were rejected under 35 U.S.C. § 102(b) as being anticipated by one or more references. Pending claims 1, 8-11, 15, and 17 were rejected under 35 U.S.C. § 103(a) for obviousness based on one or more references. Applicants respectfully request reconsideration in view of the following remarks.

Response to Rejection of Claims 1-7, 13-14, 16-18 and 23-36 under 35 U.S.C. § 102(b)

Claims 1-7, 13, 14, 16-18, and 23-36 stand rejected under 35 U.S.C. § 102 as being anticipated by Cleland, et al.. U.S. Patent No. 5,643,605 ("Cleland" hereafter) as disclosing "methods and compositions for the encapsulation of adjuvants in PLGA microspheres."

It is Applicants' position that Cleland can not anticipate, as there is at least one fundamental difference between the present claims and the cited references. In order to anticipate under 35 U.S.C. § 102, the cited reference must teach every aspect of the claimed invention either explicitly or implicitly. The issue here is whether Cleland, anticipates each and every element of Applicants' claimed invention. See MPEP § 2131 (citing *Verdegaal Bros. v. Union Oil Co. Of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987)). As elaborated in *Richardson v. Suzuki Motor Co.*, "[t]he identical invention must be shown in as complete detail as is contained in the ... claim." 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1987). Furthermore, to anticipate a claim, a reference must be enabling and describe the Applicants' claimed invention sufficiently to have placed it in possession of a person having ordinary skill in the field of the invention. *In re Paulsen*, 30 F.3d 1475, 1478, 31 U.S.P.Q.2d 1671, 1673 (Fed. Cir. 1994).

The cited reference fails to meet the standard of teaching all elements of the claimed invention, and thus does not anticipate claims 1-7, 13, 14, 16-18, and 23-36. Specifically, Cleland addresses the encapsulation of adjuvant and antigen that stimulate an immune response. The instant invention relates to use of microspheres as delivery vehicles for bioactive substances. Cleland, on the other hand, makes no reference to the encapsulation of bioactive substances or to the encapsulation where bioactivity of the substance is preserved. All of the claims and disclosures in Cleland are directed toward the release of an adjuvant or antibody; no explicit or implied reference to bioactive substances is made. Furthermore, Cleland discloses only the use of poly(D-L-lactide-co-glycolide) or PLGA and does not make

references (implicit or otherwise) to any other polymer that may form the microspheres. Additionally, Cleland spends extra effort in teaching the release of the adjuvant that is in an elaborate triphasic pattern. Therefore, Cleland fails to teach every element of the rejected claims, and thus cannot anticipate them.

Applicants respectfully submit that claims 1-7, 13, 14, 16-18, and 23-36 are not anticipated by Cleland, as there are several fundamental differences (as cited above) between the present claims and Cleland. Furthermore, the sited reference and the instant invention are different; each addresses a different need. Therefore, claims 1-7, 13, 14, 16-18, and 23-36 are fully patentable. Favorable consideration and allowance of the claims is therefore respectfully requested. Applicants respectfully request that the rejection of claims 1-7, 13, 14, 16-18, and 23-36 under 35 U.S.C. § 102(b) be withdrawn.

Response to Rejection of Claims 1, 8-11, 15, and 17 under 35 U.S.C §. 103

Claims 1, 8-11, 15, and 17 stand rejected under 35 U.S.C. § 103(a) as being "unpatentable over Cleland, *et al.*, in view of 'Improving protein therapeutics with sustained release formulation' by Putney and Burke (Putney)." Applicants respectfully submit that claims 1, 8-11, 15, and 17 are not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103 for the reasons stated below.

In essence, the Action argues a combination of references that would be obvious to take what is, at best, the general disclosures of the Cleland and Putney references and combine them in ways that would address a problem in the art, namely the encapsulation of bioactive substances in which the bioactivity of the substance is preserved. In combining references the Examiner must show by specific reference in the cited art that there was (i) a suggestion to make the combination; and (ii) a reasonable expectation that the combination will succeed. Both the suggestion and the reasonable expectation must be found within the prior art, and not gleaned from the Applicants' disclosure. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); see also *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

At most, the cited references establish that it might be "obvious to try" various combinations of ingredients. "Obvious to try" however, is not the standard for patentability under 35 U.S.C. § 103. The Federal Circuit has stated:

> In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were crucial or no direction as to which of many possible choices is likely to be successful. [citing cases]
>
> In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the invention or how to achieve it. *In re O'Farrell*, 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988).

Both "obvious to try" situations arise here. First, the Examiner cites art with disclosures too broad to render the Applicants' specific combination of steps obvious. Secondly, the Examiner has proposed a modification to one of the ingredients in one of the steps based only on a very generalized motivation of seeking the desired final product, *viz.*, the encapsulation of bioactive substances in which the bioactivity of the substance is preserved. The combination of Putney would require that the person having ordinary skill in the art perform modifications or try each of the numerous possible choices until one possibly arrived at a successful result. The reference cited gives neither an indication of which parameters are crucial, nor direction as to which of many possible choices for modification is likely to be successful.

What the Examiner seeks is to use Cleland and Putney to explore a new technology using general approaches that may be promising in a field of experimentation where the art cited contains general guidance as to the particular form of the invention or how to achieve it.

Furthermore, the Office Action merely cites to the Putney reference a teaching of general propositions and the importance of stabilizers for proteins during the encapsulation process. In fact, Putney discloses several approaches to stabilization e.g., carrier proteins and the addition of small molecules. The Putney reference gives neither an indication of which parameters are crucial, nor direction as to which of many possible choices for modification are likely to be successful. Additionally, no mention is made in the Putney reference to

"Improving protein therapeutics with sustained-release formulations" to the teachings of Cleland.

In hindsight, the Office Action ties these two references. First, the Action does not even cite or quote in the Action from the references any text that would lead a person having ordinary skill in the art to combine these two references to reach the method of the present invention. More importantly, the combination of references fails to teach at least one element of the present invention.

Furthermore, as stated in *Ex parte Haymond* 41 U.S.P.Q.2d 1217, 1220 (B.P.A.I. 1996), "we note that it is impermissible to use the claimed invention as an instruction manual or 'template' to piece together isolated disclosures and teachings of the prior art so that the claimed invention may be rendered obvious." The Board made clear that "a rejection based on Section 103 must rest on a factual basis, with the facts being interpreted without hindsight reconstruction of the invention from the prior art." Furthermore, the Board explicitly states "the examiner has the initial duty of supplying the factual basis for the rejection he advances. He may not, because he doubts that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in the factual basis." See *In re Warner*, 379 F.2d 1011, 1017, 154 U.S.P.Q. 173, 178 (C.C.P.A. 1967), cert. denied, 389 U.S. 1057 (1968).

No more and no less occurs in the present case. The Office Action finds one piece of art (Cleland) that addresses the encapsulation of adjuvant and antigen that stimulates an immune response, but makes no reference to the encapsulation of bioactive substances in which the bioactivity of the substance is preserved and adds another piece of art (Putney) that addresses general encapsulation propositions and the importance of stabilizers for proteins during the encapsulation process. This is not a teaching of the present invention.

As most recently stated in *In re Zurko,* 59 USPQ2d 1693, 1696 (Fed. Cir. 2001), "a claimed invention is unpatentable for obviousness if the differences between it and the prior art 'are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art.'" 35 U.S.C. § 103(a) (1994);

citing *Graham v. John Deere Co.*, 383 U.S. 1, 14, 148 U.S.P.Q. 459, 465 (1966). To quote the Court of Appeals for the Federal Circuit:

> With respect to core factual findings in a determination of patentability, however, the Board cannot simply reach conclusions based on its own understanding or experience -- or on its assessment of what would be basic knowledge or common sense. *Id.* at 1697.

The Office Action, however, has taken general notions having no suggestion or motivation in the references (Cleland and Putney) and reaches conclusions that are not supported in any of the references as relates to the present claims.

Therefore, it is Applicants' position that claims 1, 8-11, 15, and 17 are not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103 for the reasons stated above. Applicants respectfully submit that the claims are in condition for allowance. Applicants respectfully request reconsideration by the Examiner, withdrawal of rejections for claims 1, 8-11, 15, and 17 and advancement of the Application to allowance.

Response to Rejection of Claims 1 and 12 under 35 U.S.C. § 103

Claims 1 and 12 stand rejected under 35 U.S.C. § 103(a) as being "unpatentable over Cleland et al. in view of U.S. Patent No. 5,560,438 to Collee, et al." (hereafter "Collee"). Applicants respectfully submit that claims 1and 12 are not obvious over Collee and are, therefore, allowable under 35 U.S.C. § 103 for the reasons stated below.

First of all, Collee and the instant invention address different problems. Collee relates to a method that involves cutting and encapsulating the core sample as it enters the core barrel with an encapsulating material for maximizing the chemical integrity and, if desired, maintaining the mechanical integrity of a core sample during transport from a subterranean formation. The instant invention relates to use of microspheres formed by polymers as delivery and release vehicles for bioactive substances. As a result Collee is not relevant to the instant invention. Furthermore, Collee does not address the retention of activity post encapsulation or the release of any substances. Therefore, Collee is not analogous art and not within the Applicants' field of invention and is not pertinent to the problem the current invention is concerned with. A person having ordinary skill in the art

would not look to Collee to address the encapsulation of bioactive molecules and the retention of biological activity.

Even if the Collee reference was considered analogous art, which it is not, claims 1and 12 are not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103. The Examiner states the "Collee et al. is relied upon for the teaching that polyethylene glycol is a known encapsulating material (c 5, l 4)," therefore, as teaching general propositions of the encapsulation process. The Examiner also states that "Cleland et al. teach that more than one encapsulating material can be used in their invention, however, they do not go on to list possible encapsulating materials." The Collee reference, however, gives neither an indication of which parameters are crucial, nor possible encapsulation materials. Additionally, no mention is made in the Collee reference to the teachings of Cleland.

As discussed *supra*, "obvious to try" is not the standard for patentability under 35 U.S.C. § 103. Both "obvious to try" situations arise here. First, the Office Action cites patents with disclosures too broad and unrelated to the instant invention to render specific combinations of steps as cited in the instant application as being obvious. Secondly, the Examiner has proposed a modification to one of the ingredients in one of the steps based only on a very generalized motivation of seeking the desired final product the encapsulation of bioactive substances in which the bioactivity of the substance is preserved. Neither Collee nor Cleland give an indication of which parameters are crucial, nor do they provide any direction as to which modification may likely be successful. Therefore, the Office Action improperly ties these two references. In addition, the Office Action does not cite or quote any text from the references that would lead a skilled artisan to combine the two references to reach the method of the present invention. More importantly, the combination of references fails to teach at least one element of the present invention. There is simply no teaching of the present invention.

The Office Action has taken general notions having no suggestion or motivation in the references (Cleland and Collee) and have reached conclusions that are not supported in any of the references as they relate to the present claims.

It is Applicants' position that claims 1 and 12 are not obvious over the cited art and is, therefore, allowable under 35 U.S.C. § 103 for the reasons stated above. Therefore, Applicants respectfully submit that the claims are in condition for allowance. Applicants respectfully request reconsideration by the Examiner, withdrawal of rejections to claims 1 and 12 and advancement of the Application to allowance.

CONCLUSION

In view of the foregoing it is respectfully submitted that pending claims 1-18 and 23-36 are drawn to novel subject matter, patentably distinct from the cited references. The Examiner is therefore respectfully requested to reconsider and withdraw the outstanding rejections. In view of the foregoing remarks it is respectfully submitted that this application and all pending claims therein are in condition for allowance and such is courteously requested. Accordingly, a favorable action in the form of an early Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned for any reason that would advance the instant Application to issue. It is believed that no fee is due for this reply. If a fee is due, however, please charge this fee to our Deposit Account No. 07-0153.

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